

The Emerging Market for Long-term Nicotine Maintenance

Kenneth E. Warner, PhD; John Slade, MD; David T. Sweanor, LLB

In increasing numbers, Americans will seek to satisfy nicotine addictions through the use of novel nicotine-delivery products devoid of several of the poisons that make cigarettes so deadly. In the vanguard are tobacco industry devices that heat tobacco derivatives rather than burn tobacco, and pharmaceutical industry nicotine-replacement products, with nicotine gum and the patch now available over the counter. Ostensibly, these 2 industries have diametrically opposed objectives, the tobacco industry striving to sustain nicotine addictions, the pharmaceutical industry to end them. However, a series of technological, economic, political, regulatory, and social developments augurs a strange-bedfellows competition in which these industries will vie for shares of a new multibillion dollar long-term nicotine-maintenance market. Regulatory options range from encouraging competition to banning all nicotine-delivery devices. A more realistic approach discourages use of the most dangerous products, while making less hazardous products readily available to adults.

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ACCOUNTING for a fifth of all deaths in America,¹ the toll of tobacco is all too familiar. So, too, is the ultimate source of tobacco's toxicity: the extraordinary grip that nicotine places on its users.² Although most smokers say they want to stop, for tens of millions, efforts to quit have failed, often despite frequent attempts.³

Recognition of the tenacity of smoking and its eventual deleterious consequences has led some health professionals to question continued, complete reliance on the traditional treatment paradigm, which has regarded abstinence as the only therapeutic goal. Instead, they are cautiously considering a harm-reduction strategy that envisions a role for long-term nicotine maintenance using products that deliver nicotine without the other toxic substances in tobacco products.⁴⁻⁸

At the heart of the nicotine-maintenance concept lies the belief that, although it is not risk free,⁹⁻¹² nicotine *per se* does not directly cause most of the enormous burden of tobacco-attributable disease. Rather, it is the tobacco products themselves (and their combustion products), the vehicles that deliver nicotine, that are "dirty" and dangerous.

The avoidance of tobacco use is thus considered far more important than kicking an addiction to nicotine. For those who cannot or will not stop using nicotine, might it not be prudent to offer an alternative to tobacco products, one that satisfies their addiction while dramatically reducing their risk of disease?

This question is actually quite complicated, requiring resolution of a myriad of issues. Can consumer-acceptable products be developed that will satisfy nicotine needs without subjecting consumers to substantial health risks? (What constitutes "substantial"?) Would such products induce children who do not now use tobacco products to initiate nicotine addictions? Would they cause former smokers to relapse? To what effect? Would users of such products also use conventional tobacco products? Would the availability of alternative nicotine-

delivery devices substantially reduce the number of people who successfully become abstinent in the future? Again, to what effect? (Again, what is "substantial"?) How would the nation's drug regulatory apparatus respond?

These are not merely abstract questions. A series of technological, economic, political, regulatory, and social developments has brought us to the brink of a new market for long-term nicotine maintenance. Whether or not the health community finds this desirable, these developments mean that tobacco users are likely to have growing numbers of nicotine-maintenance options available to them soon. Some will involve no tobacco; others will use tobacco in ways not previously imagined. There are numerous patents for such devices, including an electrically fired pseudocigarette.¹³

The options that will eventually be brought to market and the conditions of their availability remain to be defined. It is here that the health community can work with the larger society and its formal policymaking apparatus to shape the future of long-term nicotine maintenance. To broaden the debate, we describe developments that are forcing the issue and consider alternative approaches to defining and regulating a future market for nicotine-maintenance products, including those that use tobacco derivatives as the vehicle for delivering nicotine and those that do not. We derive salient lessons for the emerging environment of nicotine delivery from the history of innovation in the cigarette industry.

RECENT AND ANTICIPATED DEVELOPMENTS

New technology for delivering nicotine is evolving rapidly and dramatically. Some of the technology already commercially available is very familiar, such as

From the Department of Health Management and Policy, School of Public Health, University of Michigan, Ann Arbor (Dr Warner); Department of Medicine, University of Medicine and Dentistry of New Jersey, and St. Peter's Medical Center, New Brunswick, NJ (Dr Slade); and Non-Smokers' Rights Association, Ottawa, Ontario (Mr Sweanor).

Reprints: Kenneth E. Warner, PhD, Department of Health Management and Policy, School of Public Health, University of Michigan, 109 S Observatory, Ann Arbor, MI 48109-2029 (e-mail: kwarn@umich.edu).

2 nicotine replacement therapy (NRT) products: gum (nicotine polacrilex) and the patch.^{14,15} Some new technology has been introduced but is less familiar, including 2 cigarettelike devices from the R. J. Reynolds Tobacco Company, Premier and Eclipse.¹⁶⁻¹⁸ Finally, some of the new nicotine-delivery technology is quite unfamiliar. For example, nicotine nasal spray became available as a prescription drug only last year and a nicotine inhaler has recently been approved for marketing by the Food and Drug Administration (FDA).^{19,20}

In terms of their purposes, new products from the cigarette companies and nicotine-replacement pharmaceuticals appear to be worlds apart, the former dedicated to the perpetuation of nicotine dependence, the latter to its curtailment. However, plausible developments in both product categories and in the conditions of their availability could well make the cigarette and pharmaceutical companies the strangest of bedfellows, competing vigorously for a large market of long-term nicotine maintainers. The logic underlying this statement will emerge following consideration of each industry's innovations.

NEW-GENERATION CIGARETTELIKE DEVICES AND OLD-GENERATION EFFECTS ON HEALTH

Eclipse is being test marketed in Chattanooga, Tenn, Germany (under the name HI-Q), Sweden (Inside), and Japan (AIRS). Structurally, the device is dramatically different from the conventional cigarette, especially since it burns very little tobacco-like material. A carbon fuel element, insulated with a fiberglass jacket, heats a glycerin-laden charge of reconstituted tobacco. This vaporizes material that cools to condense into an aerosol largely made up of water and glycerin droplets that, in turn, carry nicotine and other volatiles. The consumer inhales an aerosol consisting largely of water, glycerin, nicotine, and the oxides of carbon. Nicotine is delivered at about the same rate and amount as a cigarette having a Federal Trade Commission-rated yield of 0.9 mg. Carbon monoxide yield is moderately higher than that delivered by such a cigarette. Carcinogens are much lower than in most conventional cigarettes.^{17,18,21,22}

The only similar device was Eclipse's immediate predecessor, Premier, a more radical innovation that produced an aerosol from glycerin and a tobacco extract adsorbed onto alumina beads just proximal to the carbon fuel element. Introduced in 1988, Premier failed market tests and was taken off the market amid mounting pressure on the FDA to regulate it under the Food, Drug and Cosmetic Act.²³

Both Premier and Eclipse seem designed to address 2 industry problems: smokers' concerns about the health effects of smoking, especially its carcinogenic potential, and nonsmokers' concerns about environmental tobacco smoke (neither product produces much visible smoke). Both of these industry problems have been addressed, largely without success, by earlier generations of product innovation. The environmental tobacco smoke issue is of more recent vintage, and relevant innovations are fewer in number. Two were cigarettes with built-in perfume and low-smoke cigarettes, designed with special papers resulting in less visible sidestream particulate matter.^{24,25}

Health concerns drove the 2 major previous paradigm shifts in cigarette architecture: filter-tipped cigarettes in the 1950s and low tar and nicotine (t&n) cigarettes at the end of the following decade, both presented to the public as radical design changes, much like the emerging generation of devices.

Filters were the industry's response to the then newly emerging public concern about smoking's relation to lung cancer.²⁶ The cigarette companies marketed filters as trapping the dangerous components of cigarette smoke but letting the "flavor" through.²⁴ Affording smokers an apparent alternative to quitting smoking, filters rapidly became the dominant product on the market. Their introduction and marketing were quickly followed by reversal of a 2-year decline in per capita cigarette consumption in 1953 and 1954 that had resulted from new evidence linking lung cancer to smoking, which then meant unfiltered cigarettes.²³ Ironically, the most successful early filter, touted quite explicitly for its health protection properties, the Kent Micronite filter, used crocidolite asbestos as the filtering agent.^{27,28} That filter cigarettes were introduced primarily as a public relations gambit, rather than as truly less dangerous products, is suggested by the fact that some early filtered cigarettes used harsher tobaccos, so that the filtered smoke would taste like the unfiltered smoke of old.²⁶

The industry's next technological "fix" was the low t&n cigarette, marketed, often explicitly, with the theme that health-conscious smokers had the choice of either quitting smoking or switching to low t&n brands.²⁹ By 1981, low t&n cigarettes had captured a majority of the market. Medical textbooks frequently recommended their use by patients unable or unwilling to stop smoking.^{30,31}

Since then, scientists have learned that smokers who switch from regular cigarettes to low t&n brands engage in

"nicotine regulation," compensatory behavioral changes that greatly narrow the supposed gap between high- and low-yielding cigarettes. Low t&n smokers may consume more cigarettes, take larger and more frequent puffs, inhale more deeply, smoke to a shorter butt length, and subvert the technologies that lower machine-measured t&n yields (by blocking ventilation holes in filters that, unoccluded, dilute smoke by mixing it with air).^{2,32,33}

The net effect is that, consistent with smoking being a drug dependence process, the variance in smokers' blood cotinine levels is significantly smaller than the variance of nicotine deliveries indicated in cigarette advertisements.³⁴ The public is generally unaware that t&n ratings are derived from standardized machine smoking of cigarettes, in which cigarettes are puffed at a constant volume (35 mL) and at a constant interval (60 seconds). As the data on nicotine regulation demonstrate, people do not usually smoke like machines.³⁵

Low t&n cigarettes could reduce health risks if smokers did not engage in nicotine regulation to a significant degree and if they would have continued to smoke even if low t&n cigarettes were not on the market. However, most smokers who "switch down" to low t&n cigarettes do engage in nicotine regulation.^{32,33,36} Further, the availability of low t&n cigarettes has probably substantially impeded smoking cessation.^{23,37-40} On balance, therefore, low t&n cigarettes may well have increased the aggregate societal burden of smoking, primarily by reducing the number of people who would have quit in the absence of their availability, and secondarily by switchers smoking more cigarettes.²³

Cigarette use likely would be much lower today if the only products for sale were 70-mm unfiltered smokes. The introduction and diffusion of filters and then low t&n cigarettes thus clearly benefitted the industry by maintaining or increasing sales. Industry documents show that at least some industry scientists regarded low-tar cigarettes as "health-image" products, public relations gimmicks, rather than truly "health-oriented" products.³³

The introduction of Eclipse thus follows a decades-old tradition of industry product innovation in response to public concern, with the industry's apparent intent being to reduce concern and thereby maintain or expand sales. "Concern," in this instance, has a social as well as a health connotation: emitting less visible smoke, Eclipse may be less objectionable to others around the smoker, thereby further reducing the smoker's incentive to quit. More similarly moti-

vated new-generation products will likely soon appear,^{13,17} especially if Eclipse is successfully introduced or if the national tobacco settlement proposed in June⁴¹ is enshrined in federal law. The proposal includes provisions that would encourage industry innovation leading to less hazardous products.

Whether past history is relevant to the new generation of tobacco company products remains to be seen. The promise of reduced risk for confirmed smokers may be genuine this time, especially with regard to cancer. If history repeats itself, however, this ostensibly less hazardous product might sustain high levels of nicotine addiction and, on balance, increase the aggregate disease toll.

One great risk specific to low-smoke devices is that they may be deemed acceptable for use in settings in which smoking is prohibited, such as workplaces. A plausible consequence would be regular cigarette smokers' consuming these devices during work hours, when at present they do not smoke, and then continuing to smoke their regular brands outside work. The net effect would be increased exposure to nicotine and carbon monoxide, since workplace smoking bans decrease daily cigarette consumption.⁴² For people who would have quit smoking in the absence of the daytime nicotine alternative, all the risks associated with smoking would be greatly increased.

Nicotine-Containing Pharmaceuticals

Nicotine gum introduced the era of NRT pharmaceuticals in the United States in 1984, followed by patches in 1991 and nicotine nasal spray last year, with the nicotine inhaler on the marketing horizon. A nicotine-containing lozenge on a stick (like a lollipop) is also being developed.⁴³ Researchers are investigating combination therapies as well, attempting to exploit the specific virtues of the different products.⁴⁴

A major change in product distribution may be as important as the development of NRT products: over-the-counter (OTC) sale, of nicotine gum and patches thus far. Although the quit rate will be lower than that associated with using NRT under the guidance of experienced clinicians, greater NRT accessibility could more than compensate, leading to more quitting in the aggregate.⁴⁵

Over-the-counter availability will also likely increase the use of nicotine-bearing products as partial or complete *on-going* substitutes for cigarette smoking (and other tobacco product use). It will likely routinize the use of NRT products by smokers not trying to quit, to supply nicotine when they are not smoking, ei-

ther because they want to reduce their cigarette consumption or because law or custom precludes their smoking in certain locations (eg, workplaces or airplanes).^{3,46} For this use, NRT products should logically be called *nicotine-maintenance* products.

Strange Bedfellows

Through product innovation by tobacco companies, pharmaceutical companies, and other consumer products companies, and through OTC distribution of NRT products, the lines distinguishing different types of new-generation nicotine-delivery devices could eventually become blurred. More or less intentionally, each company could find itself sustaining nicotine dependence among consumers whose choices would otherwise be limited to conventional tobacco products or abstinence. Ironically, tobacco companies and pharmaceutical companies, which approach nicotine addiction from diametrically opposite positions, could find themselves in direct competition for sales of nicotine-maintenance products among the same group of consumers.

The tobacco industry would clearly vie aggressively for such sales. With a potential market in the tens of millions of consumers in the United States alone, the pharmaceutical industry would also have to seriously consider aggressive involvement in a reconceptualized nicotine-maintenance market. Drug companies are competing now with advertising campaigns for OTC gum and patches exceeding \$100 million, which would certainly pay off more handsomely if consumers used these products over a long period.^{47,48} The relative ease of the transition from focusing exclusively on nicotine replacement to contemplating a much larger market for nicotine maintenance has been hinted at in advertisements promoting a non-nicotine smoking cessation aid, CigArrest, "for those times when you want to stop smoking, *for a moment or forever*" (emphasis added).

What would be the health impact of such a market? As described above, the history of tobacco company innovation is not encouraging: previous generations of ostensibly "less hazardous" products may well have increased the aggregate harm caused by cigarettes by encouraging the maintenance of smoking rather than quitting. Still, some future mix of products could conceivably overcome enough of smoking's dangers that the cost of their substitution for cigarettes—continued dependence on nicotine—would be less than the benefit of the reduced exposure of the population to the other poisons associated with use of tobacco products.

ALTERNATIVE SCENARIOS FOR THE FUTURE AVAILABILITY OF NICOTINE

For many health professionals, contemplating competition between the tobacco and pharmaceutical industries for long-term nicotine users will generate a sense of moral repugnance. Like it or not, however, this competition will continue to develop, barring extraordinary regulatory measures (eg, the FDA's returning nicotine gum and patches to prescription-only distribution and prohibiting the marketing of any new tobacco industry products not demonstrated to be safe).

An optimal set of market and regulatory circumstances could conceivably create incentives that encourage the development of less hazardous methods of consuming nicotine. Note that we have had a market for long-term nicotine maintenance for decades: the tobacco market. Through strict regulation of nicotine in nontobacco products, and virtually no product regulation of tobacco to date, we have, essentially, granted the tobacco industry a monopoly in the nicotine-maintenance market. Reconceptualizing that market, opening it to innovative, less hazardous products introduced through competition between the tobacco and pharmaceutical industries, could conceivably satisfy the public's desire for nicotine without exacting the current enormous cost in ruined lives.

The creation and marketing of novel nicotine-delivery devices raise a myriad of possible scenarios concerning the future availability and use of both tobacco and nontobacco nicotine-bearing products. Here we summarize scenarios defined by the regulatory approach adopted. Product availability and use will also be defined by consumer demand. Without discussing this explicitly hereafter, we assume that many consumers will want to use nicotine devices characterized by convenience, reasonable price, social acceptability, and provision of a high degree of nicotine satisfaction.

Either consistently or idiosyncratically, each of the product categories—current tobacco products, new tobacco industry nicotine-delivery systems, and nicotine devices produced by the pharmaceutical (or other) industries—could be regulated according to the following options: (1) no regulation, (2) legal availability on a nonprescription basis, (3) availability by prescription only, and (4) not legally available. In addition, regulation could include limits on advertising, disclosure of information to consumers, and so on, such as the youth-oriented marketing and sales restric-

tions pertaining to cigarettes and smokeless tobacco imposed last year by the FDA.⁴⁹

Although a court has recently affirmed the FDA's authority to regulate conventional tobacco products,⁵⁰ they are currently subject to no health and safety regulation. In contrast, all pharmaceutical company innovations have been submitted to and regulated by the FDA, with efficacious nicotine-replacement products first permitted for prescription sale and then OTC, if their abuse liability is deemed low. The FDA has also asserted its authority over other nicotine-delivery devices not submitted to the agency for approval. Favor, a precursor to the new inhaler, was prohibited as an untested drug-delivery system. Similarly, the FDA determined that Masterpiece Tobacs, a chewing gum containing shredded tobacco leaf intended for use "Anytime, when you can't smoke," was a food product adulterated with an unapproved additive, tobacco.²³

The regulatory status quo is thus well defined, with 1 critical exception: innovative tobacco industry products. To date, no major tobacco company has submitted an innovation for FDA approval, and the agency has not asserted its regulatory authority when confronted with a product from a major producer. However, the FDA has been petitioned to regulate Eclipse.⁵¹ The agency was considering claiming regulatory jurisdiction over Premier before R. J. Reynolds removed it from the market.⁵² The proposed national tobacco settlement would accord the FDA regulatory authority over such devices.

A future regulatory structure for nicotine-delivery devices could continue current policy, with new tobacco industry products treated either more like conventional tobacco products or more like conventional pharmaceutical products. Alternatively, it could treat all nicotine-yielding products identically, regulating them as either prescription or nonprescription drug-delivery devices. In theory, a decision could be reached to keep government out of the nicotine market altogether, allowing a free enterprise shoot-out between the tobacco and pharmaceutical giants. As unlikely as that seems, another possibility, banning all nicotine-yielding products, is even less conceivable.

A more rational regulatory approach might be to advantage less toxic products, instead of honoring accidents of history, as at present. All currently available nicotine-delivery devices would continue to be sold, but the least toxic would be the most easily available and attractively presented, as discussed below. Such an approach could also provide

incentives, or requirements, for incremental improvements in conventional products, for instance by requiring that cigarettes be fire safe.²³

A more radical differential regulatory strategy would require reduction of the nicotine content of conventional tobacco products over several years to levels unlikely to cause or sustain addiction.⁵³ This would afford current users ample opportunity to wean themselves off of tobacco products, while simultaneously reducing the ability of tobacco products to addict future generations of children. All other nicotine-yielding products, regardless of industry of origin, would be evaluated as drug-delivery devices by the FDA, permitting only those that met a relative harm standard on the market. The harm threshold might (for example) tolerate nicotine addiction, but prohibit any other substances known or believed dangerous to health.

Under this policy, despite their delivery of toxic compounds, tobacco products could be freely sold once they were denicotined (possibly subject to age restrictions, as at present). If people really smoke for "flavor" or "taste"—the predominant tobacco industry claim—sales of tobacco products should not be affected. If, in fact, people smoke primarily to satisfy nicotine addictions, few if any consumers likely would choose to use denicotined products on a regular or even frequent basis. This may have been the experience with Next, a denicotined brand introduced by Philip Morris in the late 1980s that failed its market tests.⁵³

In addition to determining legal availability, regulatory agencies frequently regulate circumstances of manufacture, marketing, time and location of sale, and age of purchase. Current FDA regulation of cigarettes and smokeless tobacco, to protect children, focuses exclusively on just such conditions of marketing and sale.⁴⁹

Future nicotine-delivery device regulation could rely heavily on differential marketing and sale conditions to reduce the attractiveness of the most hazardous products and increase that of the least hazardous. For example, firms might be permitted to advertise, without restrictions, products that the FDA found minimally dangerous. In contrast, if permitted at all, cigarette advertisements might be limited to black-and-white block-letter factual text. Similar distinctions could be made with regard to packaging, with plain packaging required for the most dangerous products, such as cigarettes, with warning labels consuming a third to a half of the front panel of the package.^{54,55} Differential rates of excise taxation might be used to encourage consumer use of the less hazardous products.

Regardless of which of the diverse regulatory scenarios might be adopted, there is no reason to delay marketing, packaging, and sales restrictions to reduce the glamorous imagery associated with tobacco use or incremental product design changes helpful to the public's health (eg, fire safety).

TOWARD DEVELOPMENT OF A NICOTINE POLICY

The intent of a rational nicotine policy must be to deal realistically and constructively with the public health disaster wrought by the widespread use of tobacco products. An underlying premise, supported by a wealth of evidence, is that because of addiction, tobacco products exact their toll predominantly involuntarily on the part of consumers. With rare exceptions, nicotine addiction begins during childhood and adolescence; despite sincere desires to quit, many simply find the chore too difficult.

The primary goal of a new nicotine policy should remain to help everyone who wishes to be free from nicotine and tobacco to avoid addiction or achieve abstinence. Such a policy must recognize that people who are nicotine-dependent are victims of addiction and not social miscreants. They deserve a policy that acknowledges their individual dignity, the difficulty many would have in being forced to forgo nicotine, and the opportunity to continue consuming nicotine should they so desire. At the same time, children deserve the opportunity to grow up free of inducements to become addicted to nicotine. As such, the option of having minimally harmful nicotine products available to adults, in a social and policy environment that deglamorizes nicotine consumption, seems worthy of open-minded consideration.

The notion of nicotine maintenance in less harmful forms, rather than complete abstinence, is not new. Following the introduction of filtered and then low t&n cigarettes, numerous health professionals supported switching from the conventional product to the innovation.^{38,56} More recently, an oral pathologist has advocated the use of smokeless tobacco products as a less dangerous alternative for addicted cigarette smokers.⁵⁷

With hindsight, support of filtered and then low t&n cigarettes appears to have been misguided, quite possibly the cause of more rather than less disease caused by tobacco. Similarly, encouraging addicted smokers to switch to smokeless tobacco products appears shortsighted,⁵⁸ especially given the availability of the new NRT devices, the spray and the inhaler. These are far cleaner than smokeless tobacco and may satisfy nicotine needs at least as effectively.

The approach considered here—nicotine maintenance for some addicted consumers through the provision of less toxic nicotine-delivery devices—has been advocated for quite a while by a handful of prominent scientists.^{4,59,60} Nevertheless, nicotine maintenance is certain to be unpopular with many seasoned veterans of the tobacco wars. Acknowledgment of the possibility of a world in which nicotine addiction might be tolerated, and even encouraged, would be a bitter pill to swallow for many health professionals.

Stopping short of supporting a ban on cigarettes, universally recognized as implausible (and we believe undesirable), a prevalent "zero tolerance" philosophy derives in part from the accurate perception that, to date, ostensibly risk-reducing product innovations have typically had quite the opposite effect. For at least some members of the tobacco-control community, it also likely derives in part from a puritanical streak and a cynicism fed by decades of consistently dishonest and dangerous tobacco industry behavior.^{24,38,61} Such people may find completely unacceptable the tobacco industry's continuing to profit from the sale of any kind of product, especially one that perpetuates nicotine dependence.

Adoption of a nicotine maintenance policy is fraught with dangers, as well as opportunities; the 2 may occur together. For example, to compete successfully with cigarettes and other tobacco products, nicotine-only pharmaceuticals may need to be made more attractive to consumers. The current unappealing flavor of nicotine gum may have to be improved. Similarly, more efficient (rapid) means of getting nicotine into the brain may be required (eg, the new spray or inhaler). Therein lies the promise of consumer-driven shifts away from tobacco products; but the very process of making nicotine products competitive with tobacco products, from a consumer's perspective, will increase the abuse potential associated with the new products. This amplifies the need to ensure that any involved regulatory authority develops explicit objectives and criteria with both foresight and flexibility. Flexibility may prove essential to deal with failures in the domain of foresight: any regulatory system will need to make adjustments in light of actual experience.

The presence of alternatives to conventional tobacco products will influence the degree to which people seek abstinence, and there may be shifting back and forth among delivery devices. The risks faced by novices, the young, under various scenarios will have to be carefully considered as well. What may be

good policy for dealing with the current generation of tobacco users may not be so good for future generations. The opposite holds as well. For example, in the absence of consumer-acceptable alternative nicotine-delivery devices, a multi-year phaseout of nicotine in tobacco products could avoid future generations' addiction; however, it might do so at the expense of already addicted smokers ingesting more carcinogens, by smoking more low-nicotine cigarettes to satisfy their nicotine cravings. Clearly, it would be prudent for a national nicotine policy to be subject to periodic review and revision.

In any event, the absurd irony of the contemporary nicotine regulatory environment must be reversed: new pharmaceutical products currently face a long and expensive marketing approval process, while the most dangerous nicotine-delivery devices ever invented, tobacco products, are introduced and sold without regulatory impediments. In essence, the deck of competition has been stacked heavily in favor of conventional tobacco products. A manufacturer who wishes to introduce a new cherry-flavored smokeless tobacco product does so with no regulatory obstacles. If a pharmaceutical company wants to add mint flavoring to nicotine gum to make it more palatable as a nicotine-replacement product, the company must endure years of expensive regulatory hurdles. At a minimum, rationality recommends comparable treatment of the 2 situations. Certainly, the no-regulation tobacco product model is inappropriate. But the highly constrained, time-consuming, and expensive model for contemporary pharmaceuticals may be undesirable as well, effectively minimizing firms' attempts to be innovative in this challenging market environment.

A nicotine-maintenance market will emerge from the present ferment in device innovation. Its precise characteristics remain to be established. We urge the health community, and the broader public as well, to engage in thoughtful research and discussion on the nature of this market and on the characteristics it ought to have. The stakes are extraordinarily high.

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